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## Metabolic regulation of cardiac differentiation and maturation

### Grant Award Details

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Metabolic regulation of cardiac differentiation and maturation

**Grant Type:** Basic Biology V

**Grant Number:** RB5-07356

**Project Objective:** To understand the role of metabolic regulation in cardiac differentiation and maturation.

**Investigator:**

**Name:** Christian Metallo

**Institution:** University of California, San Diego

**Type:** PI

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**Disease Focus:** Heart Disease

**Human Stem Cell Use:** Embryonic Stem Cell, iPS Cell

**Award Value:** \$1,124,834

**Status:** Closed

### Progress Reports

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**Reporting Period:** Year 1

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**Reporting Period:** Year 2

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**Reporting Period:** Year 3/NCE

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### Grant Application Details

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**Application Title:** Metabolic regulation of cardiac differentiation and maturation

**Public Abstract:** Cells in the body take up nutrients from their environment and metabolize them in a complex set of biochemical reactions to generate energy and replicate. Control of these processes is particularly important for heart cells, which need large amounts of energy to drive blood flow throughout the body. Not surprisingly, the nutritional requirements of heart cells are very different than those of stem cells. This proposal will investigate the metabolism of pluripotent stem cells and how this changes during differentiation to cardiac cells. We will determine which nutrients are important to make functional heart cells and use this information to optimize growth conditions for producing heart cells for regenerative medicine and basic biology applications. We accomplish this by feeding cells nutrients (sugar, fat) labeled with isotopes. As these labeled molecules are consumed, the isotopes are incorporated into different metabolites which we track using mass spectrometry. This advanced technique will allow us to see how sugars and fat are metabolized inside stem cells and cardiac cells obtained through differentiation. We will also study the electrical activity of these heart cells to ensure that adequate nutrients are provided for the generation of cells with optimal function. Ultimately, this project will lead to new methods for producing functional heart cells for regenerative medicine and may also lead to insights into how cardiac cells malfunction in heart disease.

**Statement of Benefit to California:** Heart disease is one of the leading causes of death in California. As a result, much of the regenerative medicine community in the state and the many Californians suffering from heart failure are interested in obtaining functional heart cells from stem cells. Our work will identify the most important nutrients required to coax stem cell-derived heart cells to behave like true adult heart cells. This information will make more effective cell models for researchers and companies to study how this disease affects heart cell metabolism. Since enzymes are highly targetable with drugs, the basic scientific findings from our work will be of great interest to California biotechnology companies and can stimulate job growth in the state. Our findings will also provide insight into very specific types of genetic heart disease, and this work may lead to additional grants from federal funding sources, bringing about additional revenue and job growth in California. A better understanding of how different nutrients influence heart cell function may provide guidance into new treatment strategies for heart disease. Finally, this work will highlight the importance of diet, nutrition, and healthy heart function, providing useful information relating to public health.

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